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AUG 2 3 2002

## 510(k) Summary of Safety and Effectiveness Information

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and CFR 807.92.

The assigned 510(k) number is K013305.


Submitted by: Patrick D. Mize, Ph.D. (author)
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Date of Summary: August 22, 2002

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**Trade name**: Thrombolytic Assessment System (TAS) or Rapidpoint™ Coag Enoxaparin (ENOX) Test Card

**Common Name**: ENOX Test Card

**Classification Name**: CFR Section 21 CFR 864.7525 Class II

**Predicate Device**: K925433 Stachrom® HEPARIN ASSAY KIT

**Description of the Device**:
The RapidPoint Enoxaparin (ENOX) test is a one-step dry coagulation method performed on the RapidPoint Coag analyzer. All of the components necessary to perform the assay, with the exception of patient sample, are included in the reaction chamber of the test card.

In the ENOX test, factor X is rapidly converted to factor Xa by a specific factor X activator initiating the clotting process. Enoxaparin, from the patient's blood, complexes with antithrombin (AT), to inhibit factor Xa and lengthen the clotting time. Reported clotting times in excess of the assay cut-off indicate an enoxaparin concentration greater than or equal to 1.0 International Units per milliliter. The results generated by the ENOX test are indicative of the anticoagulant effect produced by enoxaparin in citrated arterial whole blood.

The test card formulation contains purified Factor Xa activator, calcium, phospholipid and stabilizers. Paramagnetic iron oxide particles (PIOP) are included to provide an optical detection mechanism in the presence of patient sample.

**Intended Use**

The Rapidpoint™ Coag Enoxaparin Test card (ENOX) is a qualitative test intended for exclusive use with the Rapidpoint Coag analyzer to detect the anticoagulant effects, ≥1.0 IU/mL, of the low molecular weight heparin (LMWH), Lovenox®/Clexane® (enoxaparin sodium)[1], in arterial citrated whole blood from patients with unstable angina (UA)/non-ST segment elevation myocardial infarction (NSTEMI) who may transition to percutaneous intervention (PCI). The ENOX test is intended for use either at the point of care or in the central laboratory. The device does not discriminate between values of enoxaparin below 1.0 IU/ml and the absence of drug.

The test provides information on the patient's arterial citrated whole blood response to enoxaparin by measurement of the clotting time using a factor Xa activated clotting method and should be interpreted in conjunction with other clinical data available to the clinician.

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The ENOX Test is optimized to detect the effects of enoxaparin only. The use of the ENOX test to monitor unfractionated heparin (UFH) or other low molecular weight heparins (LMWH) is contraindicated due to the different clot signatures or responses produced by each of these compounds. ENOX test results have only been validated for use in detecting the effect of enoxaparin in citrated arterial whole blood. Unfractionated heparin interferes with this test.

For *in vitro* diagnostic use only.

**Technological characteristics of the Device compared to the Predicate Device**

| Characteristic | Predicate Device | Proposed Device |
|---|---|---|
| Device | Stachrom Heparin Assay | Rapidpoint ENOX Test |
| Intended Use | Determines heparin or LMWH concentration | Detects arterial citrated whole blood anticoagulant effect of enoxaparin (a LMWH) |
| Format | Chromogenic [colorimetric] assay | Dried reagents in reaction chamber on flat test card |
| Reaction | Two-stage chemical | One-stage clotting |
| Sample type | Plasma | Arterial citrated whole blood |
| Reagent base | Antithrombin (AT), factor Xa, chromogenic substrate | Factor X activator, phospholipid, calcium chloride, PIOP |
| Reaction | Heparin in plasma complexes with AT to inactivate added factor Xa. Remaining factor Xa catalyzes release of p-nitroaniline from the substrate; Color formation is inversely proportional to heparin level | Enoxaparin (LMWH ) in blood complexes with AT to inactivate factor Xa. Factor X activator converts factor X to factor Xa, initiating clotting process. Clot formation time is related to enoxaparin (LMWH ) concentration. |
| Instrument | Spectrophotometer | RapidPoint Coag (TAS) |
| Endpoint monitored | Colorimetric reaction; Absorbance at 405 nm | Clot formation process. Clotting time in seconds |
| Test interpretation | Heparin or LMWH concentration | Qualitative. Enoxaparin $\geq$ 1.0 IU/ml Anti Xa gives clot times in arterial citrated whole blood $\geq$ 260 Secs. Clot times < 260 secs, equivocal or drug absent. |
| Quality control | Plasma control run with each set of assays | Electronic QC, and two levels of control plasma |

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**Summary of Performance Data:**
TAS ENOX cards and the TAS (Rapidpoint Coag) analyzer were used to establish the performance characteristics of the system.

## IN-HOUSE DATA

**Reproducibility**: Reproducibility studies performed using citrated plasma with and without the addition of 1.0 (anti-Xa) IU/ml enoxaparin produced the following ENOX test results.

| Enoxaparin concentration (anti-Xa IU/ml) | 0.0 | 1.0 |
|---|---|---|
| <260 Seconds | 100% | 3.5% |
| ≥ 260 Seconds | 0% | 96.5% |

Within Run reproducibility was also performed using venous citrated whole blood from single donors. A typical result for this study is presented below.

| Enoxaparin Concentration (anti-Xa IU/ml) | 0.0 | 1.0 |
|---|---|---|
| < 260 Second | 100% | 0% |
| ≥ 260 Seconds | 0% | 100% |

The ENOX test is optimized to detect the anticoagulant effect of enoxaparin. The ENOX test **should not be used** as a method to detect the effect of enoxaparin therapy when used in combination with other heparinoids, or direct thrombin inhibitors (e.g. lepirudin). For these drugs, the treating physician should refer to the pharmacokinetics section of the Prescribing Information for information on circulation clearance times. The performance characteristics of the ENOX test have not been evaluated with clinical samples containing these antithrombin agents. The use of plasma expanders (e.g. Isolyte) may cause a prolongation of clotting time to values outside the expected range, even in the absence of enoxaparin. The use of the ENOX test in cases where hemodilution is carried out is contraindicated.

The results of in vitro studies have demonstrated that lipemia does not interfere with the ENOX test results. Hematocrit values 20 - 50% do not cause significant changes in ENOX clotting times; hematocrit levels >55% may cause elongated clotting times and should be interpreted with caution.

Deficiencies in factors X, V, and prothrombin could result in a prolongation of the ENOX clotting test result even in the absence of enoxaparin in the sample. In the presence of enoxaparin, a deficiency in these factors would reflect both enoxaparin effect and prolongation caused by the deficient factor(s). Drugs that affect clotting factors in the common pathway (e.g. coumadin), including factors X, V, prothrombin and fibrinogen can affect ENOX clotting times. No testing has been performed on clinical samples with an International Normalized Ratio (INR) above 1.4.

## CLINICAL Studies

Data were obtained from a clinical trial comparing arterial citrated whole blood clot times using the ENOX card versus central laboratory measured plasma anti-Xa levels. Citrated whole blood arterial samples were collected at baseline and at peak values (within 15 minutes of dosing) after enoxaparin administration among 88 patients. The trial was conducted at 6 sites in the United States and included 27 females (31%). The mean age of the population was 61.3 years, and the mean weight was 87.3 kg. The study cohort received enoxaparin for a primary indication of coronary artery disease. All patients received a weight-adjusted dose of 0.75mg/kg IV. Samples were tested in duplicate, and the first sample was used for final analysis. The relationship between clotting time cutoff (260 secs) and 1.0 IU/ml anti-Xa value from the clinical trial data is presented in the following table.

Number of Subjects Above and Below ENOX Cutoff of 260 seconds:

| Time/anti-Xa Concentration | anti-Xa ≥1.0 IU | anti-Xa <1.0 IU |
|---|---|---|
| ≥ 260 secs | 77 | 6 |
| < 260 secs | 3 | 2 |

The sensitivity and specificity point estimates are 96.3% (95% CI of 89.4-99.2) and 25% (95% CI of 3.2-65.1) respectively. In keeping with the qualitative nature of the claim, patients with clotting times < 260 seconds are considered to have equivocal results consistent with the absence of the drug or < 1.0 IU/ml drug levels. It is recommended that physicians continue to observe patients with equivocal clotting times, and conduct alternate tests as needed.

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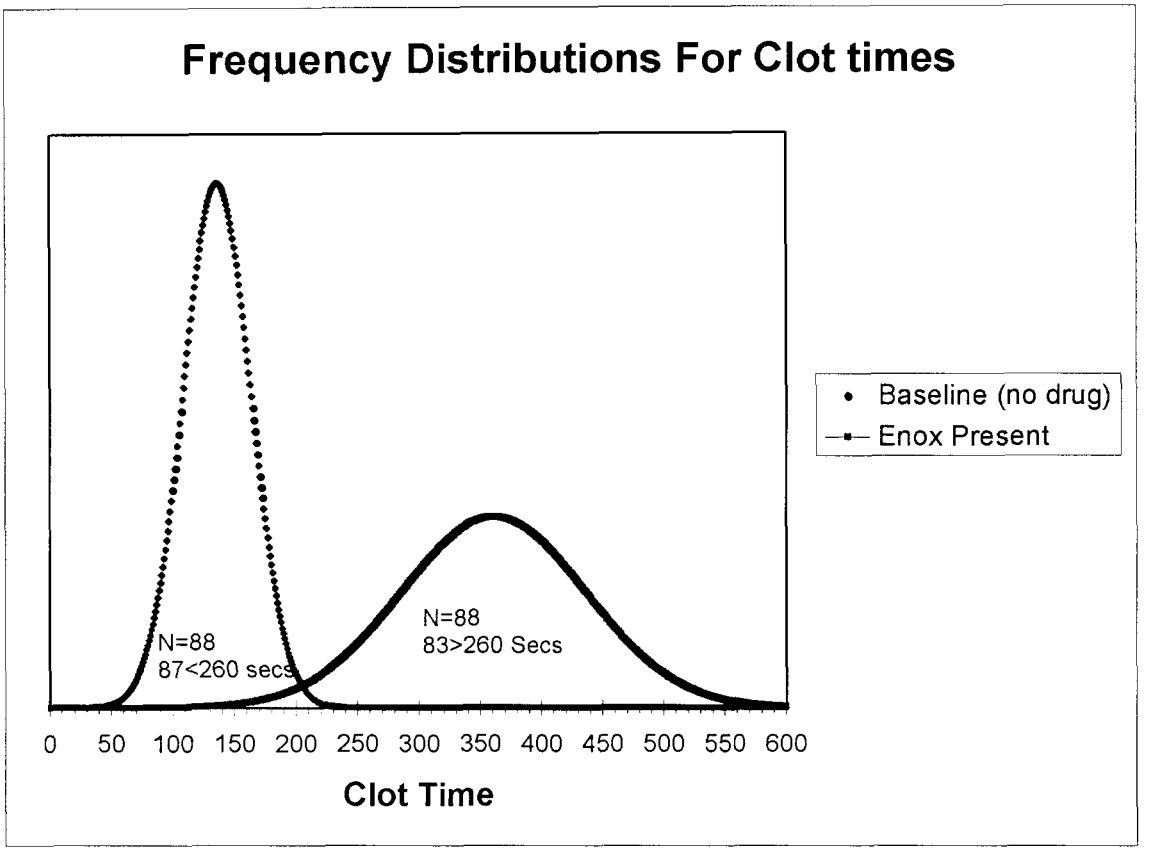


Frequency distribution of patients' ENOX card clotting times for citrated arterial whole blood samples, before and after the IV administration of Enoxaparin. The 88 patients were candidates for coronary intervention and were treated with 0.75mg/kg enoxaparin IV. Samples containing drug were obtained within 15 minutes of drug administration.

In summary, the test provides information on the patient's citrated arterial whole blood response to enoxaparin by measurement of the clotting time using a factor Xa activated clotting method. Results above the cutoff are consistent with values greater than or equal to 1.0 IU/ml of enoxaparin. The results should be interpreted in conjunction with other clinical information available to the clinician. Unexpected results should be verified with an alternative diagnostic method.

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**Statement of Substantial Equivalence**

The TAS ENOX card has been shown to be substantially equivalent to the predicate device, STACHROM® Heparin Assay, in performance, intended use and safety and effectiveness, for the qualitative determination of $\geq$ 1.0 IU/ml (anti –Xa activity) of enoxaparin in arterial citrated whole blood.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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AUG 23 2002

Ms. Laura P. Nea
Director, Quality Assurance
PharmaNetics, Inc. Cardiovascular Diagnostics, Inc.(CVDI)
9401 Globe Center Drive – Suite #140
Morrisville, North Carolina 27560

Re: k013305
Trade/Device Name: TAS ™ Enoxaparin (ENOX)™ Test Card
Regulation Number: 21 CFR 864.7525
Regulation Name: Heparin Assay
Regulatory Class: Class II
Product Code: KFF
Dated: July 18, 2002
Received: July 19, 2002

Dear Ms. Nea:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory-Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

510(k) Number (if known): K013305

Device Name: Enoxaparin (ENOX) Test Card

Indications for Use:

The Rapidpoint™Coag Enoxaparin Test card (ENOX) is a qualitative test intended for exclusive use with the Rapidpoint Coag analyzer to detect the anticoagulant effects, ≥ 1.0 IU/ml, of the low molecular weight heparin (LMWH), Lovenox®/Clexane® (enoxaparin sodium)[1], in arterial citrated whole blood from patients with unstable angina (UA)/non-ST segment elevation myocardial infarction (NSTEMI) who may transition to percutaneous intervention (PCI). The ENOX test is intended for use at either the point of care or in the central laboratory. The device does not discriminate between values of enoxaparin below 1.0 IU/ml and the absence of drug.

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(Division Sign-Off)
Division of Clinical Laboratory Devices

510(k) Number K013305

(PLEASE DO NOT WRITE BELOW THIS LINE- CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)